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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,887	07/24/2001	Dong Huang	P444 0001	3331

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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	**PAPER NUMBER**
1616	13

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/910,887	Applicant(s) HUANG ET AL.	
	Examiner Sabiha Qazi	Art Unit 1616	

-- Th MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-3,9,10,14,16 and 33-68* is/are pending in the application.

4a) Of the above claim(s) *33-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-3, 10, 14, 16,* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Acknowledgement is made of the response file in paper no. 12, dated 8/25/03. Claims 1-3, 9, 10, 14, 16 and 33-68 are pending. No claim is allowed. Instant invention is drawn to sapogenins of dammarane series. Sapogenins with no hydroxyl group at C-20 compared to sapogenins that have a hydroxyl group at C-20 are claimed to be surprisingly more effective in cancer treatment.

Since claims and claims 14 and 16 are not limited to the method of treatment disclosed in the specification rejection is maintained. New claims are part of specification where no data has been provided. For example claim 38 is drawn to method of inducing apoptosis, killing cancer cells and inhibit lung cancer cells etc. Applicant can only claim the methods, which are completely enabled by the specification, meaning that just being written in specification is not that the subject matter is enabled.

Claims 7-8, and 14, 16 and 33-68 stand rejected under 35 U.S.C. 112, first paragraph. The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation.

The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)).

Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ

367 (CCPA 1971). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988). Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: Instant invention is directed to saponins and sapogenins of dammarane series and their method of use for the treatment of cancer.

The state of the prior art: No compound has ever been found that can treat cancers generally even though massive efforts have been directed towards this end. Nearly all-anticancer drugs are effective against only a limited group of related cancers. Therefore, a compound effective against cancer generally would be a revolutionary exception.

The predictability or unpredictability of the art: There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Therefore predicting which compounds within the broad genus will be useful is impossible.

The amount of direction or guidance presented

Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991).

There is no drug, which is broadly effective against all forms of cancer, (see Carter S.K. et al. Chemotherapy of Cancer, pages 364 and 365; second edition, John Wiley & sons, New York, 1981, appendix C). See table on pages 364 and 365 where the interaction of different drugs on various type of cancer are listed. It is clear from the data that each drug has different interactions with different types of tumors i.e. one drug cannot treat all type of cancer.

See *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work.

In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result."

A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See *In re Riat* et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

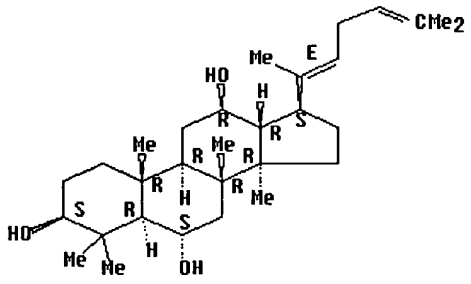
The quantity of experimentation necessary

Since different aspects of biological activity cannot be predicted but must be determined from the case to case by painstaking experimental study and when the above factors are weighed together, one of ordinary skill in the art

would be burdened with undue experimentation study. Since the nature of the method is so unpredictable, and since the claims are drawn to a broad range of pharmaceuticals for treatment of such a broad range of disease states, and since there is a lack of guidance present in the specification, the skilled artisan would have to undertake undue experimentation to practice the claimed invention commensurate with the scope of the claims.

The comparative data provided in the specification shows a comparative study however the compounds compared are not the closest prior art compounds. The closest prior art compound should differ only at 20-position having (S) configuration, because applicants are claiming same compounds differing only at 20-position by (R) configuration. See MPEP 716.02 (e).

2. Claims 1 and 2 rejected under 35 U.S.C. 102(b) as being anticipated by Park et al., See the following compound. This compound is anticipated by the prior art, see compound 12 on page 215. This compound is labeled as PAM 110 in present application.



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CN Dammara-20 (22), 24-diene-3, 6,12-triol, (3.beta.,6.alpha.,12.beta.,20E)-

Claim Rejections - 35 USC § 103

Claims 1-3, 9, 14, and 16 rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al., Yun et al. and Sung Won Kwon et al. See the

entire documents. All the references cited above teach dammarane sapogenins and saponins, which embraces Applicant's claimed invention.

1. **Determining the scope and contents of the prior art.**

Park et al. teach ginseng saponins for multidrug resistance, see the entire

document and structure of compounds cited above. Sang-Kwon et al teaches the ginsenoside Rg3 inhibition on multi drug resistance, see the entire document especially page 336 where anticancer activity of the gingenosides are disclosed; Yun et al. teaches anticarcinogenic effect and identification of active compound, Ginsenoside Rg3, Rg5 and Rh2 were found to be active anticarcinogenic compounds and they are said to prevent cancer either singularly or synergistically, see the abstract, Tables 1-8, fig. 1-3 and compounds on page S 13; Park teach ginseng saponin compounds and their use as antitumor agent. Similar sapogenins and saponins as positional isomer (double bond at different position in the side chain attached at 17-poaition) is instantly claimed. See compound at page S13, Rg5 in Yun et al. which has the following structure.

2. **Ascertaining the differences between the prior art and the claims at issue.**

Instant claims drawn to compounds and method of use differs from the references in claiming a different position of double bond in the side chain at 17-position. Even though by disclaiming certain compounds for anticipation, instant invention is considered obvious over the prior art, because instant invention is the positional isomer of the prior art.

3. **Resolving the level of ordinary skill in the pertinent art.**

Since presently claimed compounds are the positional isomer of the prior art, or saponins are known one having ordinary skilled in the art in search for

additional dammarane sapogenins or saponins would be motivated to isolate or prepare such compounds and would expect anticancer activity. Cleavage of sugar from saponins to get sapogenins is conventional and is known to one skilled in the art. This would not be a patentable distinct matter.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Since instant sapogenins and saponins are isolated from ginseng as in instant invention and posses anticancer and multi resistance properties which is considered obvious to one skilled in the art at the time of invention to prepare isomers and expecting the same properties which is taught by the prior art for similar compounds. In absence of showing any criticality or unexpected results presently claimed invention is considered obvious to one skilled in the art.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer

coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-3, 9, 10, 14, 16 provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-3, 5, 7-10, 16-23, 25, and 27-34 of copending Application No. 09/982,018. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on every business day..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The

fax phone number for the organization where this application or proceeding is assigned is 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER